

Column E Explanation Form for Regulated Species

1. Registration Number: 74-R-0072
2. Number of animals used in this study: 15
3. Species (common name) of animals used in this study: Guinea Pig
4. Explain the procedure producing pain and distress.

Guinea pigs are infected with a specific virus and develop disease symptoms such as weight loss, ruffled fur, lethargy and transient fever. The virus is an animal virus that causes these symptoms only in guinea pigs and hamsters. However, the guinea pig model is very useful for studying a related, frequently lethal, human viral disease that is characterized by high fevers and other symptoms. After infection, the guinea pigs are treated with potentially therapeutic experimental human antibodies, alone or in combination with an approved anti-viral drug. It is hypothesized that treatment with the experimental antibodies will decrease the disease symptoms and/or increase survival rates. Addition of the anti-viral drug to the treatment regimen may improve the effectiveness of the antibody therapy. As a result of the experimental treatments, symptoms resulting from the infection in the guinea pigs are generally mild. The experimental antibodies that are being tested were developed in an earlier phase of this project. Because the antibodies are not expected to elicit an adverse immune response in humans, this study is of direct relevance to the related human disease.

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results.

In the guinea pig viral model, the animals develop signs of the disease six to seven days after infection. These include fever and weight loss as viremia develops; these are the symptoms that will be followed in the experiment. If the animals are not treated, they would be expected to succumb naturally to the infection between days 12-18. In contrast, guinea pigs treated with therapeutic antibodies in these studies may exhibit less severe clinical symptoms and increased survival rates or times. The guinea pigs may experience some pain or distress at the time they display disease symptoms and thus are placed in category E. However, these symptoms are part of the normal disease progression and an important read-out of whether the anti-viral therapy is successful. Consequently, the guinea pigs are not administered analgesics or other drugs to alleviate pain or distress since such interventions would interfere with interpretation of any efficacy observed for the therapeutic antibody treatments. For animals that do develop significant clinical disease, the study endpoints allow humane euthanasia prior to severe distress so as to limit the duration of disease symptoms.

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